

Ex. 5 - Deliberative Process

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Key Deficiencies Identified in Screen:

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Differences between OX513A and *Wolbachia*-infected mosquitoes: Based on EPA's screen, EPA cannot make a finding of no exposure to humans similar to the finding for *Wolbachia*-infected mosquitoes because 1) a potentially substantive portion of the f1 generation resulting from OX513A males mating with wild females can survive to blood-feed (Fig. 1) and 2) there is a higher incidental release rate of OX513A compared to *Wolbachia* infected mosquitoes (Fig. 1). Additionally, data are not sufficient to show the tTAV and DsRed2 are not present in saliva or cannot be transmitted to humans during mosquito feeding.

Will a HSRB review be required? The *Aedes aegypti* mosquito is typically found in proximity to humans. Ergo, the proposed field trial must take place in human communities. Because trapping will be conducted indoors and there is the potential for humans to be exposed to biting mosquitoes which contain tTAV and DsRed2 (Fig. 1) the study could be subject to the Human Studies Rule, 40 CFR part 26, but more information is necessary to make that determination.

Risk associated with potential exposure: As noted, above, the data deficiencies do not provide adequate evidence for EPA to make a finding of no exposure to the pesticide. The potential risks associated with exposure to mosquitoes containing tTAV and DsRed2 proteins is a human being bitten and having a potential allergic reaction beyond the wheal typically seen with mosquito bites.

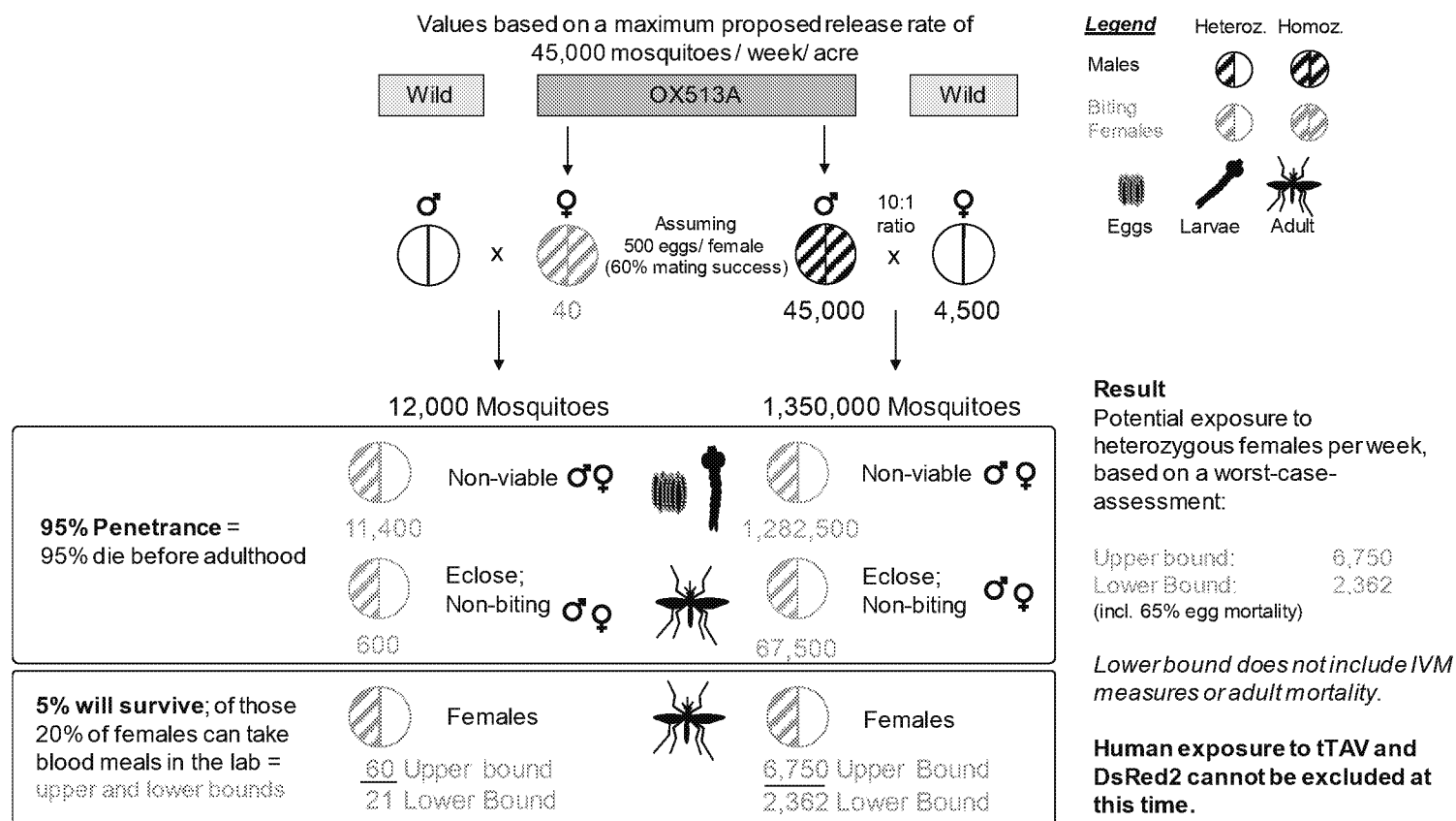


Figure 1: Worst-case scenario estimate of the potential human exposure to tTAV and DsRed2-carrying OX513A biting females in the first weeks based on proposed labeling.

Oxitec reports 95% mortality of offspring resulting from matings between homozygous OX513A mosquitoes with wild type mosquitoes. Of the surviving 5%, in laboratory conditions, 20% of females can reach adulthood, take blood meals, and lay eggs. According to the company, an *Aedes aegypti* female can lay up to 500 eggs. **Top:** Oxitec proposes a maximum release rate of 45,000 homozygous OX513A mosquitoes per week per acre. **Left:** The sex-sorting accuracy prior to releases is not 100%. The manufacturing process allows for 0.2% of released mosquitoes to be female; however, based on data provided by Oxitec, EPA expects a lower frequency (0.01 – 0.09%). Assuming a worst-case 60% mating success of these females, they may lay up to 12,000 eggs (24 x 500), which potentially results in 60 heterozygous females that may survive into adulthood (designated as upper bound, i.e., 20% of 5% surviving offspring). A more conservative approach, which we designate as lower bound, takes 65% potential egg mortality into account, which may be a more realistic number under environmental conditions. The lower bound is 21 heterozygous adult female mosquitoes. **Right:** At a release rate of 10:1 OX513A males over wild males (per Oxitec publication), and 60% mating success (assumed), 1.35 mio. mosquitoes could result from the mating with wild females. Again, of these, 95% will die from lack of tetracycline and 5% will survive. Of these 5%, 20% of the surviving females are potentially able to take blood meals and lay eggs. In this scenario, the upper bound is 6,750 heterozygous female mosquitoes, and the lower bound is 2,362. Conclusion: Human exposure to biting OX513A homozygous and heterozygous females cannot be excluded at this time.